

(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_3\text{-C}_6\text{-alkenyl}$, $\text{C}_2\text{-C}_6\text{-alkinyl}$, trifluoromethyl, $\text{C}_3\text{-C}_8\text{-cycloalkyl}$, $\text{C}_1\text{-C}_6\text{-hydroxyalkyl}$, hydroxy, $\text{C}_1\text{-C}_6\text{-alkoxy}$, $\text{C}_3\text{-C}_6\text{-alkenyloxy}$, $\text{C}_3\text{-C}_6\text{-alkinyloxy}$, benzyloxy, $\text{C}_1\text{-C}_7\text{-alkanoyloxy}$, $\text{C}_2\text{-C}_7\text{-alkoxycarbonyloxy}$, $\text{C}_1\text{-C}_6\text{-alkylthio}$, $\text{C}_3\text{-C}_6\text{-alkenylthio}$, $\text{C}_3\text{-C}_6\text{-alkinylthio}$, $\text{C}_3\text{-C}_8\text{-cycloalkyloxy}$, $\text{C}_3\text{-C}_8\text{-cycloalkylthio}$, $\text{C}_2\text{-C}_7\text{-alkoxycarbonyl}$, aminocarbonyl, $\text{C}_2\text{-C}_7\text{-alkylaminocarbonyl}$, $\text{C}_3\text{-C}_{11}\text{-dialkylaminocarbonyl}$, carboxy, phenyl, phenoxy, phenylthio, pyridyloxy, pyridylthio, and NR^5R^6 , wherein

R^5 and R^6 are selected independently of each other from the group consisting of hydrogen, $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_3\text{-C}_6\text{-alkenyl}$, $\text{C}_3\text{-C}_6\text{-alkinyl}$, benzyl and phenyl;

R^2 is selected from the group consisting of hydrogen, halogen, cyano, $\text{C}_1\text{-C}_6\text{-alkyl}$, trifluoromethyl, hydroxy, $\text{C}_1\text{-C}_6\text{-alkoxy}$, benzyloxy and $\text{C}_1\text{-C}_7\text{-alkanoyloxy}$;

R^1 and R^2 , if adjacent, may form a bridge selected from

Dr
-(CH₂)₄- and -(CH=CH)₂- or CH₂O-CR⁷R³-O-, wherein
R⁷ and R⁸ are selected independently from each other from
hydrogen and C₁-C₆-alkyl;

R³ is selected from the group consisting of hydrogen,
halogen, C₁-C₆-alkyl, trifluoromethyl and C₁-C₆-hydroxyalkyl;

R⁴ is selected from the group consisting of hydrogen, C₁-
C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₃-C₆-cycloalkyl,
hydroxy, C₁-C₆-alkoxy and benzyloxy;

Sub
E1
k is 0 or 1,

A is selected from the group consisting of
C₁-C₆-alkylene,

a substituted C₁-C₆-alkylene which is substituted one to
three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, or
phenyl,

C₂-C₆-alkylene, in which a methylene unit is isosterically
replaced by O, S, NR⁹, CO, SO or SO₂, wherein, with the
exception of CO, the isosteric substitution is not adjacent to
the amide group and R⁹ is selected from the group consisting of
hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₁-C₆-acyl
and C₁-C₆-alkanesulfonyl,

1,2-cyclopropylene,

C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once

to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, cyano or phenyl,

Sub
E1
C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano or phenyl;

1,3,5-hexatrienylene,

a 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano or phenyl, and

ethinylene,

D is selected from the group consisting of C₂-C₁₀-alkylene,

a substituted C₂-C₁₀-alkylene which is substituted once or twice by C₁-C₅-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkenylene,

a substituted C₄-C₁₀-alkenylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

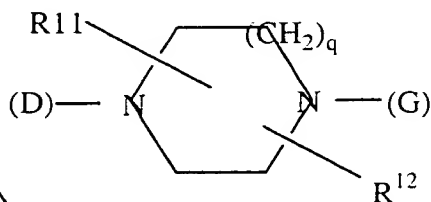
C₄-C₁₀-alkinylene,

a substituted C₄-C₁₀-alkinylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy; and

C₂-C₁₀-alkylene, C₄-C₁₀-alkenylene or C₄-C₁₀-alkinylene, in

which one to three methylene units are isosterically replaced by O, S, NR¹⁰, CO, SO, or SO₂, wherein R¹⁰ has the same meaning as R⁹, but is selected independently thereof;

E is



wherein

q is 1, 2, or 3;

R¹¹ is selected from the group consisting of hydrogen C₁-C₅-alkyl, hydroxy, hydroxymethyl, carboxy, or C₂-C₇-alkoxycarbonyl,

R¹² is selected from the group consisting of hydrogen, C₁-C₆-alkyl and an oxo group adjacent to a nitrogen atom,

and wherein R¹¹ and R¹² may together form a C₁-C₃-alkylene bridge under formation of a bicyclic ring system;

G is selected from the group consisting of G1, G2, G3, G4, and G5, wherein

Gⁱ is $-(CH_2)_r-(CR^{14}R^{15})_s-R^{13}$

r is 0, 1, 2 or 3,

s is 0 or 1,

Dr
R¹³ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₃-C₃-cycloalkyl,

saturated or unsaturated four to eight-membered heterocycles,

Sub
saturated or unsaturated four to eight-membered heterocycles which contain one or two hetero-atoms selected from the group consisting of N, S and O,

E₁
benzyl, phenyl,

monocyclic aromatic five or six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O where the heterocycles are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage may occur either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage may occur either over an aromatic ring or a hydrogenated ring and either directly or over a methylene group,

DI
 R^{14} has the same meaning as R^{13} , but is selected independently thereof;

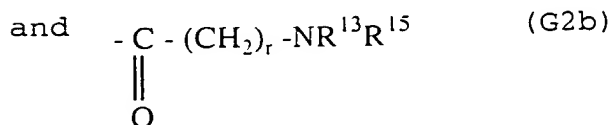
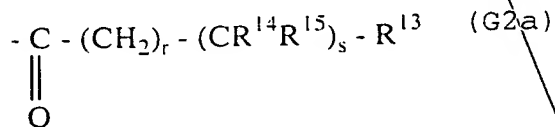
R^{15} is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, and phenyl,

Sub
E1
monocyclic aromatic five or six-member heterocycles, which contain one to three hetero-atoms selected from the group consisting of N, S and O and wherein the heterocycles are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage occurs either over an aromatic ring or a hydrogenated ring and either directly or over a methylene group,

G^2 is selected from the group consisting of



Dr
wherein r, s and the substituents R^{13} to R^{15} can have the above meaning, or the group $-NR^{13}R^{15}$ is a nitrogen containing heterocycle,

wherein $-NR^{13}R^{15}$ is a nitrogen-containing heterocycle bound over the nitrogen atom selected from the group consisting of

Sub
saturated or unsaturated monocyclic, four to eight-membered nitrogen-containing heterocycles,

E1
saturated or unsaturated monocyclic, four to eight-membered nitrogen-containing heterocycles which, aside from the essential nitrogen atom, contain one or two further hetero-atoms selected from the group consisting of N, S and O,

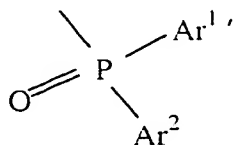
saturated or unsaturated bi- or tricyclic anellated or bridged nitrogen-containing heterocycles with 8 to 16 ring atoms,

saturated or unsaturated bi- or tricyclic anellated or bridged nitrogen-containing heterocycles with 8 to 16 ring atoms which aside from the essential nitrogen atom, contain one or two further hetero-atoms that are selected from N, S and O;

G^3 is $-SO_2-(CH_2)_r-R^{13}$

wherein r and R^{13} have the above meanings,

G^4 is



wherein

Dr
Ar¹ and Ar² are selected independently from each other from the group consisting of phenyl, pyridyl and naphthyl,

G⁵ is -COR¹⁶

Sub
R¹⁶ is selected from the group consisting of trifluoromethyl, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy, and benzyloxy,

E1
wherein G is not -(CH₂)_r-(CR¹⁴R¹⁵)_s-R¹³ when
R¹³ represents pyridyl or phenyl, which may be substituted by halogen, alkyl, alkoxy or trifluoromethyl,
R¹⁴ represents hydrogen or phenyl, which may be substituted by halogen, alkyl, alkoxy or trifluoromethyl,
R¹⁵ represents hydrogen,
A represents alkylene, substituted ethenylene or butadienylene,
D represents alkylene or alkenylene,
E represents piperazine or homopiperazine, and
s is 1;

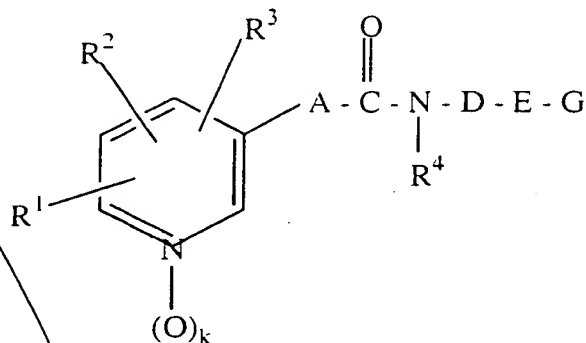
wherein G is not phenyl, N-containing heteroaryl or -(CH₂)_{ma}-CHR^{10a11a}, wherein:

R^{10a} is hydrogen or phenyl, R^{11a} is a phenyl or a pyridyl, and ma is an integer of 0 to 2, and wherein the phenyl group or moiety may be substituted by one or two members selected from the group consisting of halogen, a C₁-C₆ alkyl, trifluoromethyl and a C₁-C₆ alkoxy; when

Rⁱ is hydrogen, a halogen, a C₁-C₆-alkyl, a C₁-C₆-alkoxy, a C₁-C₆-alkylthio, a C₃-C₆-cycloalkyloxy, a C₃-C₆-cycloalkylthio, a C₂-C₇-alkoxycarbonyl, carboxy, a phenyl,

- Dr*
- Sub*
- E1*
- a phenoxy, a phenylthio, 3-pyridyloxy or 3-pyridylthio;
- R² is hydrogen, a hydroxy, a C₁-C₇-alkanoyloxy or a C₂-C₇-alkoxycarbonyloxy, or when R¹ and R₂ are adjacent to each other, they may combine to form tetramethylene or -CH₂OCR^{8a}R^{9a}O-, wherein R^{8a} and R^{9a} are the same or different and are each a C₁-C₆-alkyl;
- R³ is hydrogen, a C₁-C₆-alkyl or a hydroxy-C₁-C₆-alkyl;
- A is a C₁-C₆-alkylene or -(CR^{6a}=CR^{7a})ra-, wherein R^{6a} is hydrogen, a C₁-C₆-alkyl or a phenyl, R^{7a} is hydrogen, a C₁-C₆-alkyl, cyano or a phenyl, and ra is 1 or 2;
- R⁴ is hydrogen;
- D is a C₁-C₁₀-alkylene or a C₄-C₁₀-alkylene interrupted by at least one double bond; and
- E is selected from the group consisting of piperazine, piperazine, which is substituted by C₁-C₆-alkyl, homopiperazine, and homopiperazine, which is substituted by C₁-C₆-alkyl.

3 (Once amended) A compound according to formula (I)



(I)

wherein

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1-C_6 -alkyl, trifluoromethyl, C_3-C_8 -cycloalkyl, C_1-C_6 -hydroxyalkyl, hydroxy, C_1-C_4 -alkoxy, benzyloxy, C_1-C_4 -alkylthio, C_1-C_5 -alkanoyloxy, C_1-C_4 -alkylthio, C_2-C_5 -alkoxycarbonyl, aminocarbonyl, C_2-C_5 -alkylaminocarbonyl, C_3-C_9 -dialkylaminocarbonyl, carboxy, phenyl, phenoxy, phenylthio, pyridyloxy, and NR^5R^6 , wherein

R^5 and R^6 are selected independently of each other from hydrogen and C_1-C_6 -alkyl;

R^2 is selected from the group consisting of hydrogen, halogen, cyano, C_1-C_6 -alkyl, trifluoromethyl, hydroxy, and C_1-C_4 -alkoxy;

R^3 is selected from the group consisting of hydrogen, halogen and C_1-C_6 -alkyl;

D+
 ~~R^4 is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_3 - C_6 -cycloalkyl, hydroxy, C_1 - C_6 -alkoxy and benzyloxy;~~

~~k is 0 or 1,~~

~~A is selected from the group consisting of C_1 - C_6 -alkylene,~~

Sub
~~a substituted C_1 - C_6 -alkylene which is substituted one to three-fold by C_1 - C_3 -alkyl, hydroxy, fluorine, or phenyl,~~

E1
 ~~C_2 - C_6 -alkylene, in which a methylene unit is isosterically replaced by O, S, NR^9 , CO, SO or SO_2 , wherein, with the exception of CO, the isosteric substitution is not adjacent to the amide group and, the residue R^9 , is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_1 - C_6 -acyl and methane sulfonyl;~~

~~1,2-cyclopropylene,~~

~~C_2 - C_6 -alkenylene,~~

~~a substituted C_2 - C_6 -alkenylene which is substituted once to three-fold by C_1 - C_3 -alkyl, hydroxy, fluorine, cyano or phenyl,~~

~~C_4 - C_6 -alkadienylene,~~

~~a substituted C_4 - C_6 -alkadienylene which is substituted once to twice by C_1 - C_3 -alkyl, fluorine, cyano or phenyl;~~

~~1,3,5-hexatrienylene,~~

Dr
a substituted 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano, and

ethinylene,

Sub
D is selected from the group consisting of C₂-C₁₀-alkylene,

E1
a substituted C₂-C₁₀-alkylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy;

C₄-C₁₀-alkenylene,

a substituted C₄-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy;

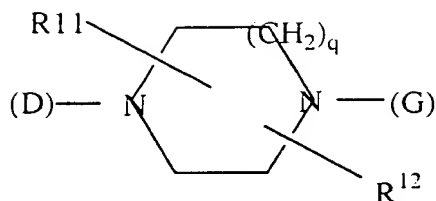
C₄-C₁₀-alkinylene,

a substituted C₄-C₁₀-alkinylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy; and

C₂-C₁₀-alkylene, C₄-C₁₀-alkenylene or C₄-C₁₀-alkinylene, wherein one to three methylene units are isosterically replaced by O, S, NR¹⁰, CO, SO, or SO₂, wherein

R¹⁰ has the same meaning as R⁹, but is selected independently thereof;

E is



wherein

q is 1, 2, or 3;

Sub
E1
R¹¹ is selected from the group consisting of hydrogen C₁-C₃-alkyl, hydroxy, hydroxymethyl, carboxy, and C₂-C₇-alkoxycarbonyl and

R¹² is selected from the group consisting of hydrogen, and an oxo group adjacent to a nitrogen atom,

and wherein R¹¹ and R¹² may together form a C₁-C₃-alkylene bridge under formation of a bicyclic ring system;

G is selected from the group consisting of G1, G2, G3, G4, and G5, wherein

G¹ is $-(CH_2)_r-(CR^{14}R^{15})_s-R^{13}$

r is 0, 1 or 2,

s is 0 or 1,

R¹³ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₃-C₆-cycloalkyl; benzyl, phenyl;

Dr
monocyclic aromatic five or six-membered heterocycles,
which contain one to three hetero-atoms selected from the
group consisting of N, S and O, wherein the heterocycles are
either bound directly or over a methylene group,

Sub
E1
anellated bi- and tricyclic aromatic or partially
hydrogenated carbocyclic ring systems with 8 to 16 ring atoms
and at least one aromatic ring, wherein the linkage occurs
either over an aromatic or a hydrogenated ring and either
directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially
hydrogenated heterocyclic ring systems with 8 to 16 ring atoms
and at least one aromatic ring, wherein one to three ring
atoms are selected from the group consisting of N, S and O,
wherein the linkage occurs either over an aromatic ring or a
hydrogenated ring and either directly or over a methylene
group,

R^{14} has the same meaning as R^{13} , but is selected
independently thereof;

R^{15} is selected from the group consisting of hydrogen,
hydroxy, methyl, benzyl, phenyl,

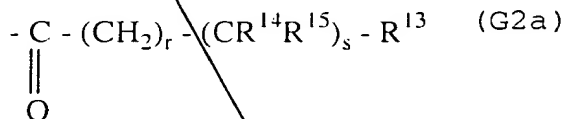
monocyclic aromatic five or six-membered heterocycles,
which contain one to three hetero-atoms selected from the
group consisting of N, S and O, wherein the heterocycles are
either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially
hydrogenated carbocyclic ring systems with 8 to 16 ring atoms

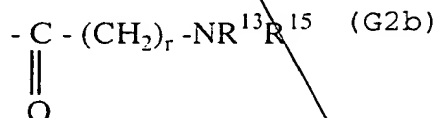
and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

aneellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms can be selected from N, S and O and the linkage may occur either over an aromatic ring or a hydrogenated ring and either directly or over a methylene group;

G² is selected from the group consisting of



and



wherein r, s and the substituents R¹³ to R¹⁵ can have the above meaning, or the group -NR¹³R¹⁵ is a nitrogen containing heterocycle,

wherein -NR¹³R¹⁵ is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle selected from the group consisting of

saturated or unsaturated monocyclic, four to eight-membered heterocycles,

saturated or unsaturated monocyclic, four to eight-membered heterocycles which aside from the essential nitrogen

atom, contain one or two further hetero-atoms selected from the group consisting of N, S and O,

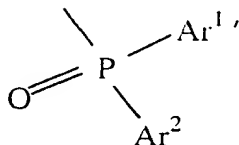
saturated or unsaturated bi- or tricyclic anellated or bridged heterocycles with 8 to 16 ring atoms, and

saturated or unsaturated bi- or tricyclic anellated or bridged heterocycles with 8 to 16 ring atoms that aside from the essential nitrogen atom, contain one or two further hetero-atoms that are selected from the group consisting of N, S and O;

G^3 is $-SO_2-(CH_2)_r-R^{13}$

wherein r and R^{13} have the above meaning,

G^4 is



wherein

Ar^1 and Ar^2 are be selected independently from each other from the group consisting of phenyl, pyridyl and naphthyl,

G^5 is $-COR^{16}$

R^{16} is selected from the group consisting of trifluoromethyl, C_1 - C_6 -alkoxy, C_3 - C_6 -alkenyloxy, and benzyloxy,

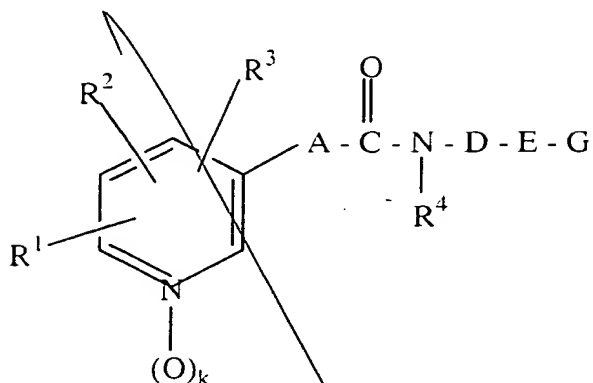
wherein G is not phenyl, N-containing heteroaryl or $-(CH_2)_{ma}-$

~~GHR^{10a}R^{11a}, wherein:~~

~~R^{10a} is hydrogen or phenyl, R^{11a} is a phenyl or a pyridyl, and ma is an integer of 0 to 2, and wherein the phenyl group or moiety may be substituted by one or two members selected from the group consisting of halogen, a C₁-C₆ alkyl, trifluoromethyl and a C₁-C₆ alkoxy; when~~

- ~~R¹ is hydrogen, a halogen, a C₁-C₆-alkyl, a C₁-C₆-alkoxy, a C₁-C₆-alkylthio, a C₃-C₃-cycloalkyloxy, a C₃-C₃-cycloalkylthio, a C₂-C₇-alkoxycarbonyl, carboxy, a phenyl, a phenoxy, a phenylthio, 3-pyridyloxy or 3-pyridylthio;~~
- ~~R² is hydrogen, a hydroxy, a C₁-C₇-alkanoyloxy or a C₂-C₇-alkoxycarbonyloxy, or when R¹ and R₂ are adjacent to each other, they may combine to form tetramethylene or -CH₂OCR^{8a}R^{9a}O-, wherein R^{8a} and R^{9a} are the same or different and are each a C₁-C₆-alkyl;~~
- ~~R³ is hydrogen, a C₁-C₆-alkyl or a hydroxy-C₁-C₆-alkyl;~~
- ~~A is a C₁-C₆-alkylene or -(CR^{6a}=CR^{7a})ra-, wherein R^{6a} is hydrogen, a C₁-C₆-alkyl or a phenyl, R^{7a} is hydrogen, a C₁-C₆-alkyl, cyano or a phenyl, and ra is 1 or 2;~~
- ~~R⁴ is hydrogen;~~
- ~~D is a C₁-C₁₀-alkylene or a C₄-C₁₀-alkylene interrupted by at least one double bond; and~~
- ~~E is selected from the group consisting of piperazine, piperazine, which is substituted by C₁-C₆-alkyl, homopiperazine, and homopiperazine, which is substituted by C₁-C₆-alkyl.~~

~~12. (three times amended) A pharmaceutical composition comprising the compound of formula (I)~~



(I)

wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_2 - C_6 -alkinyl, trifluoromethyl, C_3 - C_8 -cycloalkyl, C_1 - C_6 -hydroxyalkyl, hydroxy, C_1 - C_6 -alkoxy, C_3 - C_6 -alkenyloxy, C_3 - C_6 -alkinyloxy, benzyloxy, C_1 - C_7 -alkanoyloxy, C_2 - C_7 -alkoxycarbonyloxy, C_1 - C_6 -alkylthio, C_3 - C_6 -alkenylthio, C_3 - C_6 -alkinylthio, C_3 - C_8 -cycloalkyloxy, C_3 - C_8 -cycloalkylthio, C_2 - C_7 -alkoxycarbonyl, aminocarbonyl, C_2 - C_7 -alkylaminocarbonyl, C_3 - C_{13} -dialkylaminocarbonyl, carboxy, phenyl, phenoxy, phenylthio, pyridyloxy, pyridylthio, and NR^5R^6 , wherein

R^5 and R^6 are selected independently of each other from the group consisting of hydrogen, C_1 - C_6 -alkyl, C_3 - C_6 -alkenyl, C_3 - C_5 -alkinyl, benzyl and phenyl;

R^2 is selected from the group consisting of hydrogen, halogen, cyano, C_1 - C_6 -alkyl, trifluoromethyl, hydroxy, C_1 - C_6 -alkoxy, benzyloxy and C_1 - C_7 -alkanoyloxy;

~~D₅~~
R³ is selected from the group consisting of hydrogen, halogen, C₁-C₆-alkyl, trifluoromethyl and C₁-C₆-hydroxyalkyl;

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₃-C₆-cycloalkyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

Sub
E₂
k is 0 or 1,

A is selected from the group consisting of C₁-C₆-alkylene,

a substituted C₁-C₆-alkylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, or phenyl,

C₂-C₆-alkylene, in which a methylene unit is isosterically replaced by O, S, NR⁹, CO, SO or SO₂, wherein, with the exception of CO, the isosteric substitution is not adjacent to the amide group and R⁹ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₁-C₆-acyl and C₁-C₆-alkanesulfonyl,

1,2-cyclopropylene,

C₂-C₆-alkenylene,

a substituted C₂-C₆-alkenylene which is substituted once to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, cyano or phenyl,

C₄-C₆-alkadienylene,

~~D^x~~ a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano or phenyl;

~~1,3,5-hexatrienylene,~~

~~a 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano or phenyl, and~~

~~ethynylene,~~

~~D is selected from the group consisting of C₂-C₁₀-alkylene,~~

~~a substituted C₂-C₁₀-alkylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;~~

~~C₄-C₁₀-alkenylene,~~

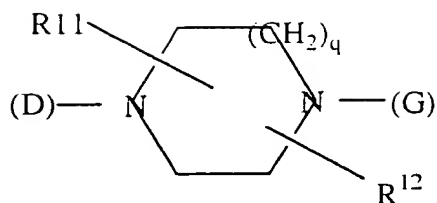
~~a substituted C₄-C₁₀-alkenylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;~~

~~C₄-C₁₀-alkynylene,~~

~~a substituted C₄-C₁₀-alkynylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy; and~~

~~C₂-C₁₀-alkylene, C₄-C₁₀-alkenylene or C₄-C₁₀-alkynylene, in which one to three methylene units are isosterically replaced by O, S, NR¹⁰, CO, SO, or SO₂, wherein R¹⁰ has the same meaning as R⁹, but is selected independently thereof;~~

E is



wherein

q is 1, 2, or 3;

~~R¹¹ is selected from the group consisting of hydrogen C₁-C₆-alkyl, hydroxy, hydroxymethyl, carboxy, or C₂-C₇-alkoxycarbonyl,~~

R¹² is selected from the group consisting of hydrogen, C₁-C₆-alkyl and an oxo group adjacent to a nitrogen atom,

G is selected from the group consisting of G1, G2, G3, G4, and G5, wherein

$$G^1 \text{ is } -(\text{CH}_2)_r-(\text{CR}^{14}\text{R}^{15})_s-\text{R}^{13}$$

r is 0 to 3,

s is 0 or 1,

R¹³ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkynyl, C₃-C₈-cycloalkyl,

saturated or unsaturated four to eight-membered heterocycles,

Sub
EQ
~~saturated or unsaturated four to eight-membered heterocycles which contain one or two hetero-atoms selected from the group consisting of N, S and O,~~

~~benzyl, phenyl,~~

~~monocyclic aromatic five or six-membered heterocycles,~~

~~monocyclic aromatic five or six-membered heterocycles which contain one to three hetero-atoms selected from the group consisting of N, S and O where the heter-atoms and are either bound directly or over a methylene group,~~

~~anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,~~

~~anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O and the linkage can occur either over an aromatic ring or a hydrated ring and either directly or over a methylene group,~~

~~R¹⁴ has the same meaning as R¹³, but is selected independently thereof;~~

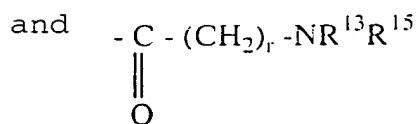
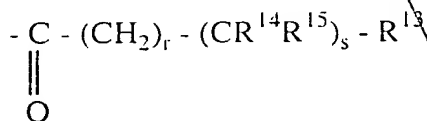
~~R¹⁵ is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, and phenyl,~~

22
 monocyclic aromatic five or six-member heterocycles,
 which contain one to three hetero-atoms selected from the
 group consisting of N, S and O and wherein the hetero-atoms
 are either bound directly or over a methylene group,

Sub
E2
 anellated bi- and tricyclic aromatic or partially
 hydrogenated carbocyclic ring systems with 8 to 16 ring atoms
 and at least one aromatic ring, wherein the linkage occurs
 either over an aromatic or a hydrogenated ring and either
 directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially
 hydrogenated heterocyclic ring systems with 8 to 16 ring atoms
 and at least one aromatic ring, wherein one to three ring
 atoms are selected from the group consisting of N, S and O and
 the linkage occurs either over an aromatic ring or a hydrated
 ring and either directly or over a methylene group,

G² is selected from the group consisting of



wherein r, s and the substituents R¹³ to R¹⁵ can have the
 above meaning, or the group -NR¹³R¹⁵,

wherein -NR¹³R¹⁵ is a nitrogen-containing heterocycle bound
 over the nitrogen atom selected from the group consisting of

32
~~saturated or unsaturated monocyclic, four to eight-membered nitrogen-containing heterocycles,~~

~~saturated or unsaturated monocyclic, four to eight-membered nitrogen-containing heterocycles which, aside from the essential nitrogen atom, contain one or two further hetero-atoms selected from the group consisting of N, S and O,~~

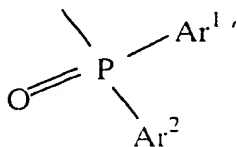
Sub E2
~~saturated or unsaturated bi- or tricyclic anellated or bridged nitrogen-containing heterocycles with 8 to 16 ring atoms,~~

~~saturated or unsaturated bi- or tricyclic anellated or bridged nitrogen-containing heterocycles with 8 to 16 ring atoms which aside from the essential nitrogen atom, contain one or two further hetro-atoms that are selected from N, S and O;~~

G^3 is $-SO_2-(CH_2)_r-R^{13}$ ($G3$)

wherein r and R^{13} have the above meanings,

G^4 is



wherein

Ar^1 and Ar^2 are selected independently from each other from phenyl, pyridyl or naphthyl,

D2
 G^5 is $-\text{COR}^{16}$ ($G5$)

R^{16} is selected from the group consisting of trifluoromethyl, $\text{C}_1\text{-C}_6\text{-alkoxy}$, $\text{C}_3\text{-C}_6\text{-alkenyloxy}$, and benzyloxy,

Sub
E2
wherein G is not $-(\text{CH}_2)_f-(\text{CR}^{14}\text{R}^{15})_g-\text{R}^{13}$ when R^{13} represents pyridyl or phenyl, substituted by halogen, alkyl, alkoxy or trifluoromethyl,

R^{14} represents hydrogen or phenyl, substituted by halogen, alkyl, alkoxy or trifluoromethyl,

R^{15} represents hydrogen,

A represents alkylene, substituted ethenylene or butadienylene,

D represents alkylene or alkenylene,

E represents piperazine or homopiperazine, and

S is 1;

wherein G^1 is not phenyl, N -containing heteroaryl or $(-\text{CH}_2)_{ma}-\text{CHR}^{10a}\text{R}^{11a}$, wherein:

R^{10a} is hydrogen or phenyl, R^{11a} is a phenyl or a pyridyl, and ma is an integer of 0 to 2, and wherein the phenyl group or moiety may be substituted by one or two members selected from the group consisting of halogen, a $\text{C}_1\text{-C}_6$ alkyl, trifluoromethyl and a $\text{C}_1\text{-C}_6$ alkoxy; when

R^1 is hydrogen, a halogen, a $\text{C}_1\text{-C}_6\text{-alkyl}$, a $\text{C}_1\text{-C}_6\text{-alkoxy}$, a $\text{C}_1\text{-C}_6\text{-alkylthio}$, a $\text{C}_3\text{-C}_8\text{-cycloalkyloxy}$, a $\text{C}_3\text{-C}_8\text{-cycloalkylthio}$, a $\text{C}_2\text{-C}_7\text{-alkoxycarbonyl}$, carboxy, a phenyl, a phenoxy, a phenylthio, 3-pyridyloxy or 3-pyridylthio;

R^2 is hydrogen, a hydroxy, a $\text{C}_1\text{-C}_7\text{-alkanoyloxy}$ or a $\text{C}_2\text{-C}_7\text{-alkoxycarbonyloxy}$, or when R^1 and R_2 are adjacent to each

other, they may combine to form tetramethylene or

$-\text{CH}_2\text{OCR}^{3a}\text{R}^{3a}\text{O}-$, wherein R^{3a} and R^{3a} are the same or

different and are each a $\text{C}_1\text{-C}_6\text{-alkyl}$;

R^3 is hydrogen, a $\text{C}_1\text{-C}_6\text{-alkyl}$ or a hydroxy- $\text{C}_1\text{-C}_6\text{-alkyl}$;

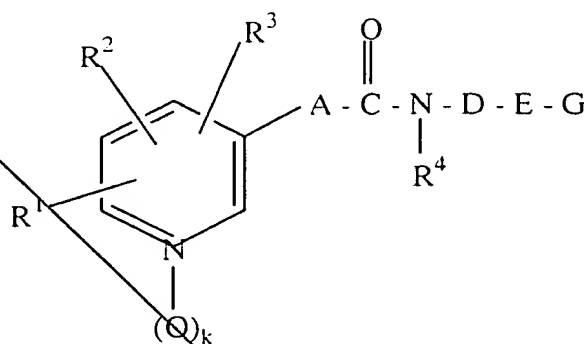
A is a $\text{C}_1\text{-C}_6\text{-alkylene}$ or $-(\text{CR}^{6a}=\text{CR}^{7a})\text{ra}-$, wherein R^{6a} is hydrogen, a $\text{C}_1\text{-C}_6\text{-alkyl}$ or a phenyl, R^{7a} is hydrogen, a $\text{C}_1\text{-C}_6\text{-alkyl}$, cyano or a phenyl, and ra is 1 or 2;

R^4 is hydrogen;

D is a $\text{C}_1\text{-C}_{10}\text{-alkylene}$ or a $\text{C}_4\text{-C}_{10}\text{-alkylene}$ interrupted by at least one double bond; and

E is selected from the group consisting of piperazine, piperazine, which is substituted by $\text{C}_1\text{-C}_6\text{-alkyl}$, homopiperazine, and homopiperazine, which is substituted by $\text{C}_1\text{-C}_6\text{-alkyl}$.

32. (once amended) A pharmaceutical composition comprising the compound of formula (I)



(I)

wherein

R^1 is selected from the group consisting of hydrogen, halogen, cyano, $\text{C}_1\text{-C}_6\text{-alkyl}$, trifluoromethyl, $\text{C}_3\text{-C}_3\text{-cycloalkyl}$, $\text{C}_1\text{-C}_6\text{-hydroxyalkyl}$, hydroxy, $\text{C}_1\text{-C}_4\text{-alkoxy}$, benzyloxy, $\text{C}_1\text{-C}_4\text{-}$

3
alkylthio, C₁-C₅-alkanoyloxy, C₁-C₄-alkylthio, C₂-C₅-alkoxycarbonyl, aminocarbonyl, C₂-C₅-alkylaminocarbonyl, C₃-C₉-dialkylaminocarbonyl, carboxy, phenyl, phenoxy, phenylthio, pyridyloxy, and NR⁵R⁶, wherein

R⁵ and R⁶ are selected independently of each other from hydrogen and C₁-C₆-alkyl;

Sub E3
R² is selected from the group consisting of hydrogen, halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, hydroxy, and C₁-C₄-alkoxy;

R³ is selected from the group consisting of hydrogen, halogen and C₁-C₆-alkyl;

R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-cycloalkyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;

k is 0 or 1,

A is selected from the group consisting of C₁-C₆-alkylene,

a substituted C₁-C₆-alkylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, fluorine, or phenyl,

C₂-C₆-alkylene, in which a methylene unit is isosterically replaced by O, S, NR⁹, CO, SO or SO₂, wherein, with the exception of CO, the isosteric substitution is not adjacent to the amide group and, the residue R⁹, is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₁-C₆-acyl and methane sulfonyl;

DB
~~1,2-cyclopropylene,~~

~~C₂-C₆-alkenylene,~~

~~a substituted C₂-C₆-alkenylene which is substituted once to three-fold by C₁-C₃-alkyl, hydroxy, fluorine, cyano or phenyl,~~

Sub
F3
~~C₄-C₆-alkadienylene,~~

~~a substituted C₄-C₆-alkadienylene which is substituted once to twice by C₁-C₃-alkyl, fluorine, cyano or phenyl;~~

~~1,3,5-hexatrienylene,~~

~~a substituted 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano, and~~

~~ethinylene,~~

~~D is selected from the group consisting of C₂-C₁₀-alkylene,~~

~~a substituted C₂-C₁₀-alkylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy;~~

~~C₄-C₁₀-alkenylene,~~

~~a substituted C₄-C₁₀-alkenylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy;~~

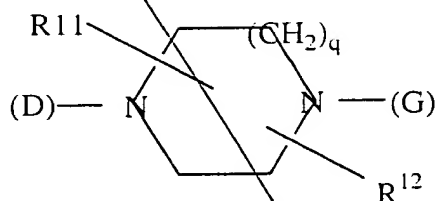
~~C₄-C₁₀-alkinylene,~~

a substituted C₄-C₁₀-alkynylene which is substituted once or twice by C₁-C₃-alkyl or hydroxy; and

C₂-C₁₀-alkylene, C₄-C₁₀-alkenylene or C₄-C₁₀-alkynylene, wherein one to three methylene units are isosterically replaced by O, S, NR¹⁰, CO, SO, or SO₂, wherein

R¹⁰ has the same meaning as R⁹, but is selected independently thereof;

E is



wherein

q is 1, 2, or 3;

R¹¹ is selected from the group consisting of hydrogen C₁-C₃-alkyl, hydroxy, hydroxymethyl, carboxy, and C₂-C₇-alkoxycarbonyl and

R¹² is selected from the group consisting of hydrogen, and an oxo group adjacent to a nitrogen atom,

and wherein R¹¹ and R¹² may together form a C₁-C₃-alkylene bridge under formation of a bicyclic ring system;

G is selected from the group consisting of G1, G2, G3,

23
G4, and G5, wherein

G¹ is $-(CH_2)_r-(CR^{14}R^{15})_s-R^{13}$

r is 0, 1 or 2,

s is 0 or 1,

Sub
E3
R¹³ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkynyl, C₃-C₆-cycloalkyl; benzyl, phenyl;

monocyclic aromatic five or six-membered heterocycles, which contain one to three hetero-atoms selected from the group consisting of N, S and O, wherein the heterocycles are either bound directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group,

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms are selected from the group consisting of N, S and O, wherein the linkage occurs either over an aromatic ring or a hydrogenated ring and either directly or over a methylene group,

R¹⁴ has the same meaning as R¹³, but is selected

independently thereof;

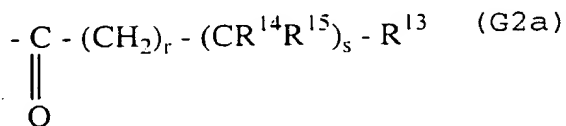
D3
 R^{15} is selected from the group consisting of hydrogen, hydroxy, methyl, benzyl, phenyl,

Sub
 monocyclic aromatic five or six-membered heterocycles, which contain one to three hetero-atoms selected from the group consisting of N, S and O, wherein the heterocycles are either bound directly or over a methylene group,

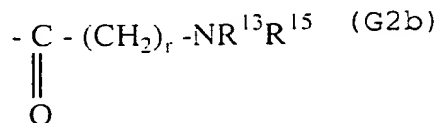
E3
 anellated bi- and tricyclic aromatic or partially hydrogenated carbocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein the linkage occurs either over an aromatic or a hydrogenated ring and either directly or over a methylene group, and

anellated bi- and tricyclic aromatic or partially hydrogenated heterocyclic ring systems with 8 to 16 ring atoms and at least one aromatic ring, wherein one to three ring atoms can be selected from N, S and O and the linkage may occur either over an aromatic ring or a hydrogenated ring and either directly or over a methylene group;

G^2 is selected from the group consisting of



and



wherein r , s and the substituents R^{13} to R^{15} can have the

~~above meaning, or the group $-NR^{13}R^{15}$ is a nitrogen containing heterocycle,~~

~~wherein $-NR^{13}R^{15}$ is a nitrogen-containing heterocycle bound over the nitrogen atom, the nitrogen-containing heterocycle selected from the group consisting of~~

~~saturated or unsaturated monocyclic, four to eight-membered heterocycles,~~

~~saturated or unsaturated monocyclic, four to eight-membered heterocycles which aside from the essential nitrogen atom contain one or two further hetero-atoms selected from the group consisting of N, S and O,~~

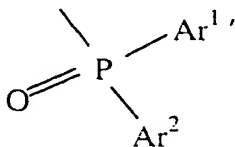
~~saturated or unsaturated bi- or tricyclic anellated or bridged heterocycles with 8 to 16 ring atoms, and~~

~~saturated or unsaturated bi- or tricyclic anellated or bridged heterocycles with 8 to 16 ring atoms that aside from the essential nitrogen atom, contain one or two further hetero-atoms that are selected from the group consisting of N, S and O;~~

G^3 is $-SO_2-(CH_2)_r-R^{13}$

wherein r and R^{13} have the above meaning,

G^4 is



wherein

DS
Ar¹ and Ar² are be selected independently from each other from the group consisting of phenyl, pyridyl and naphthyl,

G⁵ is -COR¹⁶

Sub
R¹⁶ is selected from the group consisting of trifluoromethyl, C₁-C₆-alkoxy, C₃-C₆-alkenyloxy, and benzyloxy,

E3
wherein G is not phenyl, N-containing heteroaryl or (-CH₂)_{ma}-CHR^{10a}R^{11a}, wherein:

R^{10a} is hydrogen or phenyl, R^{11a} is a phenyl or a pyridyl, and ma is an integer of 0 to 2, and wherein the phenyl group or moiety may be substituted by one or two members selected from the group consisting of halogen, a C₁-C₆ alkyl, trifluoromethyl and a C₁-C₆ alkoxy; when

R¹ is hydrogen, a halogen, a C₁-C₆-alkyl, a C₁-C₆-alkoxy, a C₁-C₆-alkylthio, a C₃-C₈-cycloalkyloxy, a C₃-C₈-cycloalkylthio, a C₂-C₇-alkoxycarbonyl, carboxy, a phenyl, a phenoxy, a phenylthio, 3-pyridyloxy or 3-pyridylthio;

R² is hydrogen, a hydroxy, a C₁-C₇-alkanoyloxy or a C₂-C₇-alkoxycarbonyloxy, or when R¹ and R₂ are adjacent to each other, they may combine to form tetramethylene or -CH₂OCR^{8a}R^{9a}O-, wherein R^{8a} and R^{9a} are the same or

different and are each a C₁-C₆-alkyl;

R³ is hydrogen, a C₁-C₆-alkyl or a hydroxy-C₁-C₆-alkyl;

A is a C₁-C₆-alkylene or -(CR^{6a}=CR^{7a})_{ra}-, wherein R^{6a} is hydrogen, a C₁-C₆-alkyl or a phenyl, R^{7a} is hydrogen, a C₁-C₆-alkyl, cyano or a phenyl, and ra is 1 or 2;

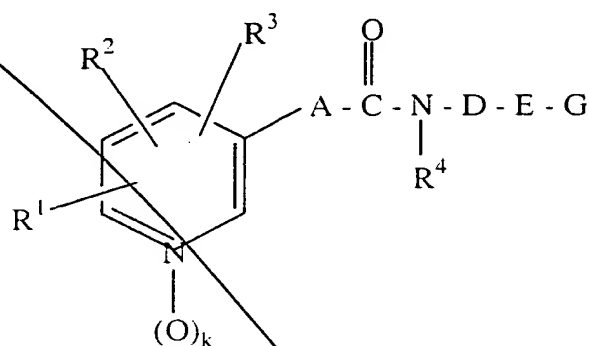
R⁴ is hydrogen;

Sub
E3
D3

- D is a C₁-C₁₀-alkylene or a C₄-C₁₀-alkylene interrupted by at least one double bond; and
- E is selected from the group consisting of piperazine, piperazine, which is substituted by C₁-C₆-alkyl, homopiperazine, and homopiperazine, which is substituted by C₁-C₆-alkyl.

D4

37. (once amended) A method for production of compounds according to formula (I)

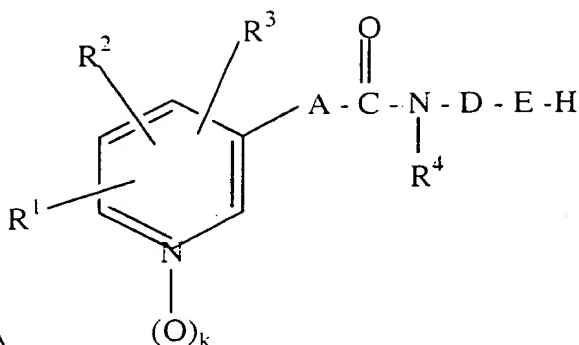


Sub
ES

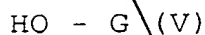
(I)

wherein G is selected from the group consisting of an acyl residue, a carbamoyl residue, a sulfonyl residue and a phosphinoyl residue,

wherein compounds of a formula



are reacted with a compound of formula (V)



wherein G is selected from the group consisting of acyl residues, carbamoyl residues, sulfonyl residues, phosphinoyl residues, and their reactive derivatives, wherein:

R^1 is selected from the group consisting of hydrogen, halogen, cyano, $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_3\text{-C}_6\text{-alkenyl}$, $\text{C}_2\text{-C}_6\text{-alkinyl}$, trifluoromethyl, $\text{C}_3\text{-C}_8\text{-cycloalkyl}$, $\text{C}_1\text{-C}_6\text{-hydroxyalkyl}$, hydroxy, $\text{C}_1\text{-C}_6\text{-alkoxy}$, $\text{C}_3\text{-C}_6\text{-alkenyloxy}$, $\text{C}_3\text{-C}_6\text{-alkinyloxy}$, benzyloxy, $\text{C}_1\text{-C}_7\text{-alkanoyloxy}$, $\text{C}_2\text{-C}_7\text{-alkoxycarbonyloxy}$, $\text{C}_1\text{-C}_6\text{-alkylthio}$, $\text{C}_3\text{-C}_6\text{-alkenylthio}$, $\text{C}_3\text{-C}_6\text{-alkinylthio}$, $\text{C}_3\text{-C}_8\text{-cycloalkyloxy}$, $\text{C}_3\text{-C}_8\text{-cycloalkylthio}$, $\text{C}_2\text{-C}_7\text{-alkoxycarbonyl}$, aminocarbonyl, $\text{C}_2\text{-C}_7\text{-alkylaminocarbonyl}$, $\text{C}_3\text{-C}_{13}\text{-dialkylaminocarbonyl}$, carboxy, phenyl, phenoxy, phenylthio, pyridyloxy, pyridylthio, and NR^5R^6 , wherein

R^5 and R^6 are selected independently of each other from the group consisting of hydrogen, $\text{C}_1\text{-C}_6\text{-alkyl}$, $\text{C}_3\text{-C}_6\text{-alkenyl}$, $\text{C}_3\text{-C}_6\text{-alkinyl}$, benzyl and phenyl;

R^2 is selected from the group consisting of hydrogen,

~~Sub
ES~~
halogen, cyano, C₁-C₆-alkyl, trifluoromethyl, hydroxy, C₁-C₆-alkoxy, benzyloxy and C₁-C₇-alkanoyloxy;

~~R³ is selected from the group consisting of hydrogen, halogen, C₁-C₆-alkyl, trifluoromethyl and C₁-C₆-hydroxyalkyl;~~

~~R⁴ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₃-C₆-cycloalkyl, hydroxy, C₁-C₆-alkoxy and benzyloxy;~~

~~k is 0 or 1,~~

~~A is selected from the group consisting of C₁-C₆-alkylene,~~

~~a substituted C₁-C₆-alkylene which is substituted one to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine, or phenyl,~~

~~C₂-C₆-alkylene, in which a methylene unit is isosterically replaced by O, S, NR⁹, CO, SO or SO₂, wherein, with the exception of CO, the isosteric substitution is not adjacent to the amide group and R⁹ is selected from the group consisting of hydrogen, C₁-C₆-alkyl, C₃-C₆-alkenyl, C₃-C₆-alkinyl, C₁-C₆-acyl and C₁-C₆-alkanesulfonyl,~~

~~1,2-cyclopropylene,~~

~~C₂-C₆-alkenylene,~~

~~a substituted C₂-C₆-alkenylene which is substituted once to three-fold by C₁-C₃-alkyl, hydroxy, C₁-C₃-alkoxy, fluorine,~~

24
cyano or phenyl,

Sub
Es
C₄-C₆-alkadienylene,

a substituted C₄-C₆-alkadienylene which is substituted once or twice by C₁-C₃-alkyl, fluorine, cyano or phenyl;

1,3,5-hexatrienylene,

a 1,3,5-hexatrienylene which is substituted by C₁-C₃-alkyl, fluorine, cyano or phenyl, and

ethinylene,

D is selected from the group consisting of C₂-C₁₀-alkylene,

a substituted C₂-C₁₀-alkylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

C₄-C₁₀-alkenylene,

a substituted C₄-C₁₀-alkenylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy;

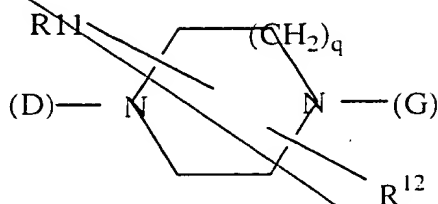
C₄-C₁₀-alkinylene,

a substituted C₄-C₁₀-alkinylene which is substituted once or twice by C₁-C₆-alkyl, hydroxy, or C₁-C₆-alkoxy; and

C₂-C₁₀-alkylene, C₄-C₁₀-alkenylene or C₄-C₁₀-alkinylene, in which one to three methylene units are isosterically replaced

by O, S, NR^{10} , CO, SO, or SO_2 , wherein R^{10} has the same meaning as R^9 , but is selected independently thereof;

E is



wherein

q is 1, 2, or 3;

R^{11} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl, hydroxy, hydroxymethyl, carboxy, or C_2 - C_7 -alkoxycarbonyl,

R^{12} is selected from the group consisting of hydrogen, C_1 - C_6 -alkyl and an oxo group adjacent to a nitrogen atom.